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# Gabapentin as an Adjunct to Decrease Opioid Consumption

Bethany L. Myhre

# GABAPENTIN AS AN ADJUNCT TO DECREASE OPIOID CONSUMPTION

by

Bethany L. Myhre

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## Abstract

**Title:** Gabapentin as an Adjunct to Decrease Opioid Consumption

**Background:** Pain is an individualized experience and controlling it can be a burden after surgery. Opioids, or narcotics, are the staple of controlling pain after surgery, but there are undesirable side effects. With the current opioid epidemic, many patients are also nervous about becoming addicted to opioids. Multi-modal anesthesia is emerging in attempts to block the pain pathway at different points and pain receptors. Gabapentin is an anti-seizure medication often used as an analgesic for chronic neuropathies and migraines. By binding to the alpha-2 delta subunit of the voltage-gated calcium channel, there is a decrease in excitatory neurotransmitters such as glutamate and substance P. Since gabapentin works on the inflammatory pathway, it is thought by giving preemptively, the pain pathway is disrupted, and post-operative opioid use may decrease.

**Purpose:** The purpose of this independent project is to present a case report and provide a comprehensive review of evidence-based literature to determine if gabapentin is effective in reducing post-op opioid use.

**Process:** By accessing the University of North Dakota Health Sciences Library, a literature search was completed through several databases including CINHAL, PubMed, Scopus, Medline Complete, EBSCO, ClinicalKey, and HealthSource. Other related literature was acquired from bibliographies of the initial articles found. All articles utilized were examined for their relation to the topic.

**Results:** There were many meta-analysis and systematic reviews relating to gabapentin administered pre-operatively and its effect on post-operative opioid use. Gabapentin was consistently found to reduce opioid consumption at 24 hours post-operatively, as well as

decrease pain scores, decrease nausea and improve patient satisfaction. Sedation was the only side effect noted but did not occur with every patient. Gabapentin may be beneficial when utilized with other non-opioid analgesics. Studies have not shown an optimal pre-op dose of gabapentin, so more research needs to be completed.

**Implications:** Anesthesia providers strive to make patients as comfortable as possible and gabapentin is showing promise in decreasing post-op opioid consumption, as well as improving pain scores. With minimal side effects and drug interactions, gabapentin can safely be administered pre-operatively.

**Keywords:** gabapentin, pain, narcotic, surgery

Gabapentin as an Adjunct to Decrease Opioid Consumption

## Background

Controlling pain after surgery continues to be a burden, despite the advances in healthcare. Pain is a complex and individualized experience. There are different types of pain that ensue when nociceptors are stimulated. Types of pain include somatic, visceral, neuropathic and inflammatory. Somatic pain is considered sharp, localized pain, whereas visceral pain is diffuse and vague. Neuropathic pain develops when damage to peripheral or central neural structures occurs which causes abnormal processing. Lastly, inflammatory pain develops when sensitization of the nociceptive pathway occurs from mediators at the site of inflammation. All types of pain are perceived differently (Nagelhout & Elisha, 2018). Having the ability to block pain perception or disrupt the way pain is processed should enable patients to heal faster, have improved satisfaction, and essentially improve the cost of care (Penprase, Brunetto, Dahmani, Janaqi Forthosffer, & Kapoor, 2015). Additionally, intense acute pain may lead to the development of chronic pain, so ensuring pain is controlled post-op is a priority (Li, Guo, Li, & Yang, 2017).

A growing concern in the country is opioid, or narcotic, addiction and many people fear becoming addicted to narcotics after surgery. Adequate pain control is essential for all patients, but especially for patients going home the same day of surgery. Narcotics are typically used for moderate to severe pain, but common adverse side effects include nausea, vomiting, pruritis, urinary retention, and respiratory depression (Liu, Liu, & Wang, 2017). If health care providers can lower pain intensity, there may be less narcotics used, thus less side effects. Multi-modal analgesia has been gaining popularity, even though the notion has been around for almost 100 years (Nagelhout & Elisha, 2018). By using different mechanisms of action to act on a variety of

pain related receptors, a synergistic effect should occur and limit narcotic usage (Kremer & Griffis, 2018). To help reduce post-operative pain and opiod use, gabapentin has been prescribed pre-operatively by some anesthesia professionals.

## Purpose

The purpose of this independent project is to present a case report of a patient undergoing general anesthesia who received gabapentin pre-operatively and observe the amount of post-op opioid used. Additionally, a review of literature was completed to gather evidence-based research to determine if gabapentin is effective in decreasing post-op opioid consumption and understand its mechanism of action.

## Case Report

A 41-year-old, 177-cm, 97.3 kg, African-American female presented to the operating room for a bilateral breast reduction. Past medical history included a N-STEMI, coronary artery disease, hypertension, hyperlipidemia, and former smoker (quit a month before surgery). She had no known medication allergies but had seasonal allergies. Current medications included lisinopril, carvedilol, Lipitor, and melatonin. Prior anesthesia was for cardiac stent placement, in which she had no complications. No known family history of anesthetic problems. Cardiac echocardiogram showed an ejection fraction of 60% and her electrocardiogram (EKG) displayed normal sinus rhythm with an old septal infarct. Pertinent labs included a negative pregnancy test, hemoglobin 12.7 g/dL, hematocrit 38.7%, platelets 162,000 μ/L, potassium 4.3 mE/L, and creatinine 0.86 m/dL.

Airway assessment revealed a Mallampati II, thyromental distance greater than three fingerbreadths, mouth opening greater than three fingerbreadths, full intact dentition and full neck range of motion. Nothing by mouth status was 10 hours. The patient was given an

American Society of Anesthesiologists (ASA) physical class of 2. Pre-op vital signs were blood pressure 133/90 mmHg, heart rate 63 beats per minute, respiratory rate 16 breaths per minute, oxygen saturation 99% on room air, and temperature 36.6º Celsius. Her physical assessment revealed regular heart tones and rhythm and clear bilateral breath sounds. Pre-op medications included 600 milligrams (mg) gabapentin by mouth (PO), 1000 mg acetaminophen PO, and 3.125 mg carvedilol PO.

After being brought into the operating room via cart, the patient transferred herself onto the operating table. Standard non-invasive monitors were placed on the patient, which included a 5-lead EKG, finger oximetry, a bi-spectral (BIS) index monitor, and a blood pressure cuff was applied to her left calf due to the nature of the surgical procedure. An 18-gauge IV had been placed in the day unit and Lactated Ringer's infusing. A mask was gently placed over the patient's mouth and nose which had oxygen flowing at 10 liters per minute (lpm). At that time, 2 mg versed and a dexmedetomidine bolus of 38 micrograms (mcg) was administered intravenously (IV). Pre-oxygenation was completed for three minutes and the patient had an end-tidal oxygen saturation of 88%.

For induction, 200 mcg fentanyl, 40 mg lidocaine, and 200 mg propofol was administered intravenously. Mask ventilation was easy without an oral adjunct. With no eyelid reflexes present, the patient's eyes were taped for corneal abrasion prevention and 50 mg rocuronium IV was given. A Macintosh 3 blade was utilized for intubation, and a 7.0 mm endotracheal tube was placed. Placement was confirmed with end-tidal $CO_2$ and auscultation of bilateral breath sounds. The tube was secured with tape. Desflurane was started and an end expiration concentration of 6.5% was achieved. The patient was placed on volume control ventilation with a tidal volume of 550 ml, rate of 9, and PEEP of 5. A nasopharyngeal temperature probe was placed for

continuous temperature monitoring during the procedure. The patient's heart rate increased to the 140's shortly after induction. BIS monitor showed adequate depth of anesthesia at 35%, with 0.9 MAC. An additional 150 mcg fentanyl IV was administered with no change. At that time, 5 mg of metoprolol IV was given, and the heart rate decreased to 80 beats per minute. An additional 16 gauge IV was placed in the right hand and secured with a transparent dressing.

During maintenance, desflurane was continued at an end expiration concentration of 6.5% and a dexmedetomidine continuous IV infusion was at 0.4 mcg/kg/hr. A lower body air warmer was initiated. Prior to incision, 2 g Ancef was given IV. Intravenous anti-emetics administered after induction included 4 mg ondansetron and 4 mg dexamethasone. A total of 25 mg of ephedrine was given intravenously to maintain systolic blood pressure greater than 100 mmHg and mean arterial pressure (MAP) greater than 65 mmHg. An additional 50 mcg of IV fentanyl was given during the case.

Close to the end of the procedure, neuromuscular blockade was checked with a train of four nerve stimulator. A 4/4 response was noted on the orbicularis oculi muscle. To ensure full neuromuscular blockade antagonism, 3 mg of IV neostigmine was given. To prevent muscarinic side effects of neostigmine, 0.2 mg of IV glycopyrrolate was administered. Procedure duration was four hours. A total of 2150 ml of Lactated Ringer's was administered during the case and an additional dose of 4 mg IV ondansetron was given. Blood loss was estimated at 200 ml and urine output was 985 ml.

Once the dressings were placed and the patient was adequately reversed, desflurane was discontinued, 100% FiO2 was administered with the oxygen flow rate increased to 8 lpm. A subglottal suction catheter was introduced, and excess sputum removed. Once the patient had adequate spontaneous ventilation volumes of 4 ml/kg, opened her eyes, and squeezed hands to

command, the endotracheal tube was removed. Four liters of oxygen was applied via nasal cannula. The patient was transferred to the post-anesthetic recovery room (PACU) via cart and patient stated she was comfortable. Ten minutes after arrival to the PACU, another 4 mg of ondansetron was given IV for nausea. An hour later, 50 mcg IV fentanyl was given for 5/10 pain. After an hour and a half in the recovery room, 10 mg oxycodone was administered orally. The patient's pain was well-controlled at 3/10 and discharged home 2 hours and 15 minutes after PACU arrival.

## Literature Search

### PICO Question

Not every anesthesia provider administers gabapentin pre-operatively and its use remains controversial in controlling post-op pain. To simplify finding clinically relevant literature, a PICO question was formed. PICO stands for population (P), intervention (I), comparison (C), and outcome (O). By constructing a PICO question, answers to health care related issues are sought by providing an effective search of evidence-based literature (Stillwell, Fineout-Overhold, Melnyk, & Williamson, 2010). The PICO question constructed is: among adult patients undergoing elective surgery (P), does the administration of gabapentin pre-op (I) compared to those not receiving gabapentin (C) have a decrease in opioid use post-op (O)?

Prior to the literature search, inclusion and exclusion criteria was determined. Articles reviewed were evaluated using Melnyk and Fineout-Overholt's *Evidence-based Practice in Nursing and Healthcare: A Guide to Best Practice* (Stillwell et al., 2010). This provides a guide to levels of hierarchy in nursing research. Study strengths are illustrated by a pyramid and allows the determination of the strength of a recommendation. Level I is considered the highest level and includes systematic reviews of randomized controlled studies, as well as meta-analysis

reviews. In order to find the appropriate randomized control trials, the researchers filter the results. The lowest level is VII, which is evidence from reports by expert committees. The highest level of evidence reduces bias and provides strength to the recommendations. Most of the literature utilized for this project was level I.

**Databases**

After the PICO question was formulated, The University of North Dakota Health Sciences Library was accessed to search several databases for pertinent literature. Databases searched included CINHAL Complete, Medline Complete, EBSCO Megafile, HealthSource: Nursing/Academic Edition, ClinicalKey, Scopus and PubMed. These databases were chosen because they cover nursing research, as well as medical research. Both need to be reviewed, as anesthesia is viewed from the nursing and medical standpoint.

**Vocabulary and Limits**

To obtain relevant articles, key words from the PICO question were utilized. The search included the key words *gabapentin*, *pain*, *narcotic*, and *surgery*. Keywords were used together when searching the databases, as the results when only two or three keywords were combined had an overwhelming number of articles. The searches were limited to full text review, meta-analysis, and randomized control trial articles in journals within the past five years, human subjects, and the English language.

The first search was performed using Scopus. There was an extensive number of articles found related to the use of gabapentin as an adjunct for pain control. This proved to be a limitation of the search as a total of 65 related articles were found. After review of relevant articles, the *similar articles* link was accessed. This resulted in fewer articles, but the articles did

not review administration of gabapentin alone. For that reason, none of the articles in Scopus were utilized.

PubMed generated 21 articles and ClinicalKey resulted in 22 articles. Several articles in those searches were duplicates, but six articles provided high quality reviews relevant to this independent project. The National Library of Medicine, which includes CINHAL, Medline, EBSCO, and HealthSource, generated 16 articles. From this database, four of the articles were relevant to the topic of gabapentin and the reduction of opioid use.

Another search was conducted utilizing PubMed to gain a better understanding of the mechanism of action of gabapentin. Keywords used were *gabapentin, mechanism of action, and pain*. Limitations included articles within the last five years and full text articles. A total of 471 articles were found. After reviewing the first displayed articles, an informative article's *similar articles* link was accessed. This yielded 44 results. Four articles provided general information on gabapentin, as well as the advantages of controlling pain. This information was utilized for explaining the background and pain pathway of gabapentin.

## Review of Literature

### Pain Pathway

In order to understand how to modulate the pain pathway, a basic understanding of the pathway is necessary. A nociceptor is a sensory neuron or first order neuron. When a noxious stimulus, such as a surgical incision, occurs on peripheral nociceptors, it is changed into an action potential. Simultaneously, chemical mediators and excitatory neurotransmitters are released, such as Substance P, glutamate, bradykinin, histamine, serotonin, prostaglandin, cytokines, and calcitonin gene-related peptide causing an inflammatory response. The action

potential is transmitted through first order neurons to the dorsal root ganglia of the spinal cord, generally by fast A-delta fibers or slow C-fibers (Nagelhout & Elisha, 2018).

Transmission of the pain impulse travels through the ascending pathway, also referred to as the spinothalamic tract or second order neurons, which synapse with third order neurons in the brain. Processing and pain perception occur in several areas of the brain, including the thalamus, reticular formation, and somatosensory area of the cerebral cortex. After processing, a response is transmitted back to the spinal cord through the descending pathway. The descending pathway modulates the ascending pathway through the periaqueductal gray area, nucleus raphe magnus, and locus coeruleus by attempting to suppress pain transmission that occurs in the dorsal horn of the spinal cord (Nagelhout & Elisha, 2018).

Sensitization of nociceptors occurs both in the peripheral and central pathway (Butterworth, Mackey, & Wasnick, 2013). This results in hyperalgesia, or increased sensitivity to pain, and allodynia, or a normally non-painful stimulus becomes painful (Butterworth et al., 2013). There are many excitatory and inhibitory neurotransmitters in the pain pathway. Excitatory neurotransmitters, which were aforementioned, make pain more intense, whereas inhibitory neurotransmitters try to block pain (Nagelhout & Elisha, 2018). Neurotransmitters produce their effect when they act on specific receptors.

**Gabapentin**

Gabapentin was first developed as an anti-seizure medication but has an off-label use for chronic pain, such as neuropathies and migraines (Rivken & Rivken, 2014). Structurally, gabapentin is a gamma-aminobutyric acid (GABA) analog but does not bind to GABA receptors. The exact mechanism of action for reducing pain is unknown, but research is providing a better understanding of how the medication works. The most widely accepted theory is that gabapentin

modulates the pre-synaptic alpha-2 delta sub-unit of voltage-gated calcium channels (Rivkin & Rivkin, 2014).

Once gabapentin is bound to the calcium channels in the nerve terminals, calcium is unable to enter the neuron, which inhibits the release of neurotransmitters such as glutamate and substance P (Alles et al., 2017). Both these substances participate in pain promotion and wind-up pain. Glutamate is an excitatory neurotransmitter that acts on the N-methyl-D-aspartate (NMDA) receptor (Nagelhout & Elisha, 2018). Once the NMDA receptor becomes activated, nitric oxide increases and excitatory amino acids are released. These cause sharp, fast pain (Butterworth et al., 2013). Substance P is a peptide released from afferent C-fibers and is involved with inflammatory pain. When an incision is made, an inflammatory response begins. Substance P causes mast cell degranulation and histamine release. This process also activates peripheral nociceptors. Plasma protein extravasation occurs causing vasodilation, edema and additional release of bradykinin (Barrett, Barman, Brooks, & Yaan, 2019).

Studies have shown gabapentin exerts its effects at the peripheral nerve terminals, as well as the spinal cord, thalamus and cortical level (Alles & Smith, 2019). Synaptic transmission is attenuated by primary afferent neurons and second order neurons in the spinal dorsal horn by decreasing glutamate release (Alles et al., 2017). With less glutamate, the NMDA receptor is unable to be activated and the transmission from peripheral sensory neurons to second order neurons is interrupted (Tomic, Pecikoza, Micov, Vuckovic, & Stepanovic-Petrovic, 2018). The excitatory drive has also been seen to decrease in the post-synaptic excitatory currents in the substantia gelatinosa (Alles et al., 2017; Tomic et al., 2018). By affecting these areas, the brainstem and medulla alter the descending nociceptive processing at the spinal level and promote the supraspinal modulation of pain (Alles & Smith, 2019). Depression of the reticular

formation and limbic system, which deal with the emotional experience of pain, has also been seen (Alles et al., 2017).

By exerting its effects in the dorsal horn of the spinal cord to reduce substance P, gabapentin prevents peripheral and central sensitization when administered prior to insult (Tomic et al., 2018). In addition, the inflammatory pain was decreased to a greater extent in a preventative setting versus when the inflammatory process had already begun (Tomic et al., 2018). This was evidenced by a decrease in edema and neutrophil infiltration to the area of incision (Tomic et al., 2018).

**Pre-operative Gabapentin**

Numerous studies have been completed with gabapentin administered pre-operatively and the observation of post-op opioid consumption. With many randomized control trials completed, there have been several systematic reviews and meta-analysis of administration of pre-op gabapentin and the relationship it has with post-op opioid use, pain scores, patient satisfaction and adverse side effects.

Alayed, Alghanaim, Tan, and Tulandi (2014) completed a systematic review of 14 randomized controlled trials of patients undergoing abdominal hysterectomies where some women received pre-op gabapentin, and others received a placebo. A total of 900 patients were included. Cumulative morphine doses were compared post-op, as well as pain scores based on the visual analog scale (VAS). A significant reduction in opioid use was found with the gabapentin group at 24 hours. Patients who received gabapentin also had a decrease in their VAS score. An interesting find was the addition of several doses of gabapentin administered post-operatively had no significant effect on VAS scores, deciding that gabapentin is favorable for pre-op administration (Alayed et al., 2014).

Steinberg et al. (2017) also reviewed randomized control trials of abdominal hysterectomies and the use of gabapentin preemptively. The researchers assessed gabapentin solely, as well as combined with other pre-operative analgesics. Their systematic review determined the use of gabapentin with the addition of acetaminophen used fewer narcotics than gabapentin alone. This conclusion supports the theory of analgesics having a synergistic effect on pain control. Satisfaction scores among those who received gabapentin as an intervention were higher than those who did not receive gabapentin. The length of stay was no different between the control and intervention group.

Other systematic reviews and meta-analysis have been completed which also show patients who receive gabapentin pre-operatively have a reduction in opioid use, a decrease in pain scores, and an increase in patient satisfaction (Doleman et al., 2015; Li et al., 2017; Mao, Wu, & Ding, 2016). Doleman et al. (2015) reviewed 133 studies which had a large amount of heterogeneity in surgeries but concluded the type of surgery was not a factor in opioid consumption but the subjective experienced pain by the patient. In other words, the effect of gabapentin post-op was independent of the surgical procedure. Not only did gabapentin decrease post-op opioid consumption and improve pain scores, but chronic pain at three months post-op was reduced (Doleman et al., 2015).

Gabapentin was found to be less effective when administered with spinal anesthesia (Doleman et al., 2015). This finding was consistent with Mao, Wu, and Ding's (2016) review of patients undergoing total hip arthroplasties where some patients received spinal anesthesia with gabapentin and others received only spinal anesthesia. There was no difference in VAS scores at rest or mobilization between patients who received gabapentin pre-op and those who did not (Mao, Wu, & Ding, 2016).

Not only is spinal anesthesia common with hip arthroplasties, but also with total knee arthroplasties. A meta-analysis performed by Zhai, Song, and Liu (2016) analyzed six clinical studies, which included 769 patients who received gabapentin pre-operatively, and observed its effects. Unfortunately, the results were not broken down into the type of anesthesia administered. A combination of spinal and general anesthesia was used. Results showed a decrease in post-op opioid use for those who received gabapentin, as well as a decrease in VAS scores (Zhai, Song, & Liu, 2016). Although opioid use was lower, there was no difference when patients were mobilized (Zhai, Song, & Liu, 2016).

Li et al. (2017) looked at 12 randomized control trials which included 938 patients undergoing laparoscopic cholecystectomies and compared opioid usage between those who received gabapentin pre-op and those who did not. Opioid consumption was reduced, as well as pain scores both at rest and with mobilization. With a lower pain level, patients may mobilize sooner and ultimately have an earlier discharge, decreasing the cost of care (Li et al., 2017). One item which makes this meta-analysis unique is researchers observed the dose-effect relationship between gabapentin and VAS scores. A positive correlation was found between the two. As the dose of gabapentin increased, the VAS scores improved (Li et al., 2017).

A comparative study including 83 women was completed to evaluate outcomes of patients undergoing bilateral breast reduction surgery using a multi-modal, narcotic free approach with IV sedation versus a traditional general anesthetic with opioids (Parsa et al., 2017). Although this study does not specifically discuss gabapentin given alone pre-operatively, it does include gabapentin as part of a multi-modal approach to analgesia. The multi-modal approach utilized celecoxib and gabapentin pre-operatively and acetaminophen post-operatively for pain control. Both groups received lidocaine as the local anesthetic intra-operatively.

Surprisingly, the opioid-free group used less narcotics in the recovery room, had less incidence of nausea, and had quicker discharge times. The theory behind the results is the body's natural opioids, beta-endorphins, are stimulated with incision which help with post-op pain control. Beta-endorphins have been said to be 18 to 33 times more potent than opioids (Parsa et al., 2017). There were several limitations to the study but shows consistency with systematic review results demonstrating gabapentin can reduce post-op narcotic use.

## Discussion

A common theme among the systematic reviews and meta-analysis was gabapentin reduced post-op opioid use in the first 24 hours, decreased pain scores, and decreased nausea. The only major side effect associated with administration of gabapentin was sedation (Alayed et al., 2014; Doleman et al., 2015). This may be beneficial, as pre-operative anxiety may be reduced. The optimal dose is yet to be determined as gabapentin dosing ranged from 300 mg to 1200 mg PO in the randomized control trials. Li et al. (2017) found higher doses were superior to low doses of gabapentin, but there also was a positive correlation between the dose and sedation.

After receiving 600 mg of PO gabapentin an hour and a half before surgery, the patient presented to the operating room fully awake and did not complain of being drowsy but did feel relaxed. Literature states to use a "normal" amount of narcotic intra-op (Steinberg et al., 2017); therefore, narcotic use during surgery was not decreased due to pre-op gabapentin administration. In the recovery room, she only needed a single dose of IV opioid. It is unknown what she was prescribed at discharge, but studies reviewed only observed IV consumption, not oral. She did, however, require an additional dose of ondansetron shortly after PACU arrival even though a dose was given with emergence. She was discharged home quickly, which indicates she should have been comfortable, both with her pain and nausea.

Providing adequate pain relief is a priority for anesthesia professionals. Through the review of literature, the recommendation is 600 mg of gabapentin PO be administered two hours pre-op to those undergoing elective surgeries. Since the use of multi-modal analgesia has synergistic effects, the addition of 1000 mg of acetaminophen PO administered pre-op is also recommended. Gabapentin is not metabolized by the liver, which minimizes drug-drug interactions (Barrett et al., 2019). Assessment of kidney function is necessary as the drug is excreted by the kidneys unchanged. If one's creatinine is elevated, a 300 mg PO dose may be administered, or gabapentin could be abandoned altogether.

In order to determine if a recommendation is strong or not, the Strength of Recommendation Taxonomy scale was utilized. The quality, quantity, and consistency of evidence is evaluated, and patient-oriented outcomes are emphasized (Ebell et al., 2004). An A-level grade is the best and is based on consistent evidence (Ebell et al., 2004). The lowest grade is a C-level grade, which can be an opinion, usual practice, or consensus based (Ebell et al., 2004). After review of the strength of recommendation algorithm, the administration of gabapentin pre-op has patient-oriented evidence and systematic reviews have shown consistent results. This recommendation would receive an A grade. The research for multi-modal analgesia is still emerging and one review article suggested the addition of either acetaminophen or celecoxib with gabapentin (Steinberg et al., 2017). Based on this conclusion, the strength of recommendation would receive a grade of C. The research did not specifically discuss gabapentin in relation to kidney function, so this recommendation would also receive a C grade.

With the implementation of administering pre-op gabapentin, the hope is to reduce the amount of opioid use post-op. Since gabapentin has shown to also reduce pain scores after surgery, patient satisfaction increases. Healing ultimately may occur quicker, reducing the

number of infections and decreasing the cost of care. In today's healthcare, all those factors are important, and hospitals have been attempting to improve all of them.

## Conclusion

After an extensive review of literature, it appears gabapentin administered pre-operatively decreases the amount of opioids used post-operatively. Along with the decrease of opioids, pain scores were lowered, adverse side effects were reduced, and patient satisfaction improved. More research with larger sample sizes needs to be completed to determine the optimal pre-op dose. With the current opioid epidemic and patients fear of becoming addicted to opioids, research has shown gabapentin to be effective in decreasing post-op narcotic use, which is beneficial for patients undergoing surgeries.

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# Appendix A

## Gabapentin as an Adjunct to Decrease Opioid Consumption

Bethany Myhre, SRNA

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## Introduction

- Pain control after surgery is a burden
- Types of pain
  - Somatic
  - Visceral
  - Neuropathic
  - Inflammatory
- Importance of pain control
  - Faster healing
  - Decrease infections
  - Improved patient satisfaction
  - Decrease chance of chronic pain
  - Decrease healthcare costs
- Opioids
  - Moderate to severe pain
  - Adverse side effects
- Multi-modal analgesia
  - Pre-op gabapentin

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## Case Information

- Bilateral Breast Reduction
- 41-year-old
- 97 kg
- Female
- ASA 2
- NKDA
  - Seasonal allergies

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## Pre-operative Evaluation

- Past Medical History
  - N-STEMI
  - Coronary artery disease
  - Hypertension
  - Hyperlipidemia
  - Former smoker
- Surgical History
  - Cardiac stent placement
- Current Medications
  - Lisinopril, carvedilol, Lipitor, melatonin
- Pre-op VS
  - BP 133/90 mmHg
  - HR 63/min
  - RR 16/min
  - SpO2 97% RA
  - T 36.6° C

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## Pre-operative Evaluation

- Pertinent labs
  - Negative pregnancy test
  - Hgb 12.7 g/dL
  - Hct 38.7%
  - Plt 162,000 µ/L
  - Potassium 4.3 mE/L
  - Cr 0.86 m/dL
- EKG
  - NSR with old septal infarct
- ECHO
  - EF 60%
- Airway Evaluation
  - Mallampati II
  - TMD > 3 fingerbredths
  - Mouth opening > 3 fingerbredths
  - Full intact dentition
  - Full neck range of motion
- NPO 10 hours

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## Anesthetic Course

- Medications
  - Pre-op: 600 mg gabapentin, 1000 mg acetaminophen, 3.125 mg carvedilol
  - Induction: 2 mg versed, 38 mcg dexmedetomidine bolus over 10 minutes, 200 mcg fentanyl, 40 mg lidocaine, 200 mg propofol, 50 mg rocuronium
  - Maintenance: desflurane end expiration concentration of 6.5%, 0.4 mcg/kg/hr dexmedetomidine infusion, 4 mg ondansetron, 4 mg dexamethasone, 2 g cefazolin
- General anesthetic
  - Duration
  - No nerve monitoring

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## Intraoperative Issues

- After Induction:
  - HR increased to 140's
    - 150 mcg fentanyl
    - 5 mg metoprolol
  - Additional 16 g IV
- Maintenance
  - BP decreased
    - Total of 25 mg ephedrine
- Emergence
  - 3 mg neostigmine
  - 0.2 mg glycopyrrolate
  - 4 mg ondansetron
- Totals
  - LR 2150 ml
  - EBL 200 ml
  - UO 985 ml
  - Duration 4 hours

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## PACU

- Medications
  - 4 mg ondansetron
  - 50 mcg fentanyl for 5/10 pain
  - 10 mg oxycodone
- Discharged after 2 hours and 15 minutes post-op
- Pain 3/10

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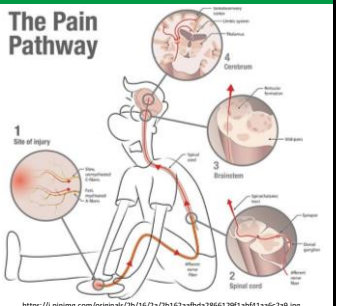
## Pain Pathway

- First Order Neurons
  - Nociceptor
    - Transmitted by A-delta or C fibers
- Second Order Neurons
  - Spinothalamic tract
- Third Order Neurons
  - Processing and pain perception
  - Thalamus, reticular formation, and somatosensory area of the cerebral cortex
- Descending pathway
  - Periaqueductal gray area, nucleus raphe magnus, and locus coeruleus

(Nagelhout & Elisha, 2018)

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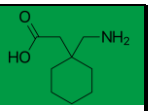
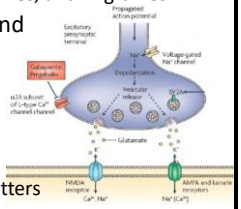
## Gabapentin




- Anti-seizure medication
  - Used for chronic pain, neuropathies, and migraines
- GABA analog, but does not bind to GABA receptors
- Mechanism of action
  - Modulates pre-synaptic alpha-2 delta sub-unit of voltage-gated calcium channels
  - Inhibits release of neurotransmitters
    - Glutamate and Substance P



(Alles et al. 2017; Barrett, Barman, Brooks, & Yaan, 2019; Nagelhout & Elisha 2018; Rivken & Rivken, 2014)
(Image: https://accessmedicine-mhmedical-com.ezproxylr.med.und.edu/ViewLarge.aspx ?figid =175219023&gbosContainerID=0&gbosid=0&groupID=0)

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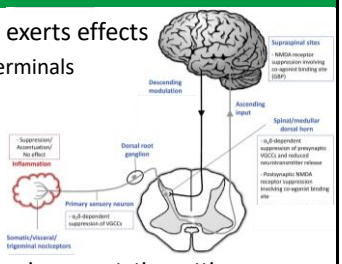
## Gabapentin cont.

- Where gabapentin exerts effects
  - Peripheral nerve terminals
  - Spinal cord
  - Thalamus
  - Cerebral cortex
- Inflammatory Inhibition
  - Pain decreased more in preventative setting




(Alles & Smith, 2019; Alles et al., 2017; Tomic, Pecikoza, Micov, Vuckovic, & Stepanovic-Petrovic, 2018. Image: Katzung, Kruidering-Hall, & Trevor, 2019)

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## Pre-op Gabapentin

- Abdominal Hysterectomy
  - Alayed, Alghanaim, Tan, & Tulandi (2014)
    - Patients who received gabapentin pre-op had significant reduction in post-op opioid use and decrease in visual analog scale (VAS) in first 24 hours
    - Additional doses of gabapentin post-op had no significant effect on VAS scores
  - Steinberg et al. (2017)
    - Gabapentin with the addition of acetaminophen used less narcotics than gabapentin alone
    - Satisfaction scores among those who received gabapentin were higher than those who did not receive gabapentin
    - No difference in length of stay

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## Pre-op Gabapentin cont.

- Doleman et al. (2015)
  - Reduction in opioid use post-op, decrease in pain scores, and increased patient satisfaction
  - Type of surgery was not a factor in the patient's pain experience
  - Chronic pain at three months was reduced
  - Less effective with spinal anesthesia
- Mao, Wu, & Ding (2016)
  - Reviewed total hip arthroplasties
    - No difference in VAS scores at rest or with mobilization
- Zhai, Song, & Liu (2016)
  - Reviewed total knee arthroplasties
    - Combination of spinal and general anesthesia with pre-op gabapentin
    - Decrease in post-op opioid use and VAS scores for those who received gabapentin
    - No difference in VAS scores when patients mobilized

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## Pre-op Gabapentin cont.

- Li et al. (2017)
  - Reviewed laparoscopic cholecystectomies
    - Reduction in post-op opioid use and pain scores at rest and at mobilization
    - Observed dose-effect relationship between gabapentin and VAS scores
      - As dose increased, VAS scores improved
- Parsa et al. (2017)
  - Small comparative study of 83 women undergoing bilateral breast reduction surgery
    - Narcotic free approach vs. traditional GA approach
    - Opioid free group used less opioids in the recovery room, less nausea, and quicker discharge times

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## Recommendations

- 600 mg gabapentin administered 2 hours pre-op for elective surgeries
- 1000 mg acetaminophen pre-op
- Reduced dose of 300 mg or no gabapentin with patients with kidney problems

(Barrett et al. 2019)

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## Conclusion

- Patient received 600 mg gabapentin 1 ½ hours pre-op
  - No complaints of drowsiness, but felt relaxed
  - Normal amount of opioids given intra-op
  - Needed single dose of IV fentanyl post-op
  - Discharged just over 2 hours post-op

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## Conclusion

- After review of administration of gabapentin pre-op
  - Reduction of opioids post-op
  - Decreased pain scores
  - Decreased nausea
  - Increased patient satisfaction
  - Adverse side effect: sedation
  - No optimal dose, so more studies need to be completed

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